



KANSAS DRUG UTILIZATION REVIEW NEWSLETTER

Health Information Designs, LLC

3rd Quarter 2019

Welcome to the Quarterly edition of the "Kansas Drug Utilization Review Newsletter", published by Health Information Designs, LLC (HID). This newsletter is part of a continuing effort to keep the Medicaid provider community informed of important changes in the Kansas Medical Assistance Program (KMAP).

Helpful Web Sites

KMAP Web Site

<https://www.kmap-state-ks.us/>

KDHE-DHCF Web Site

<http://www.kdheks.gov/hcf/>

KanCare Web Site

<http://www.kancare.ks.gov/>

Fee-For-Service (FFS)

Helpful Numbers

Provider Customer Service (Provider Use Only)

1-800-933-6593

Beneficiary Customer Service

1-800-766-9012

KMAP PA Help Desk

1-800-285-4978

In This Issue:

Hemophilia

Hemophilia

Hemophilia is a genetic blood disorder due to a deficiency of specific clotting factors. Goals of therapy are to prevent bleeding episodes and to stop bleeding if it occurs. The most common types of hemophilia are type A (classic hemophilia) and type B (Christmas disease), which are deficient in factors VIII and IX respectively.¹⁻²

Hemophilia affects 400,000 patients worldwide, or 1 in 10,000 births. Hemophilia type A is the most prevalent, affecting 1 in 5,000 births (80-85%), followed by type B affecting 1 in 30,000 births. The disease affects males predominantly, while females are carriers. Females rarely show symptoms of hemophilia but can if they are deficient in both factor VIII and IX or if they only have one X chromosome (Turner syndrome). Most commonly hemophilia is a genetic disorder that is X-linked recessive.¹⁻²

The usual clinical presentation is common in those with the following symptoms:¹⁻²

- Ecchymosis: easy bruising
- Hemarthroses: bleeding into joint spaces that mainly affects the knee, ankle, and elbow; patient will experience joint pain, swelling, erythema (70-80% of patients)
- Hematomas: collection of blood outside blood vessels, often at muscles; patient will experience pain, swelling, and decreased range of motion (ROM) (10-20% of patients)
- Hematuria: blood in urine
- Signs of nerve compression
- Oral bleeding with trauma, excessive bleeding in surgery
- Intracranial hemorrhage that can be spontaneous or post-trauma; may lead to stroke or increase in intracranial pressure (<5% of patients)

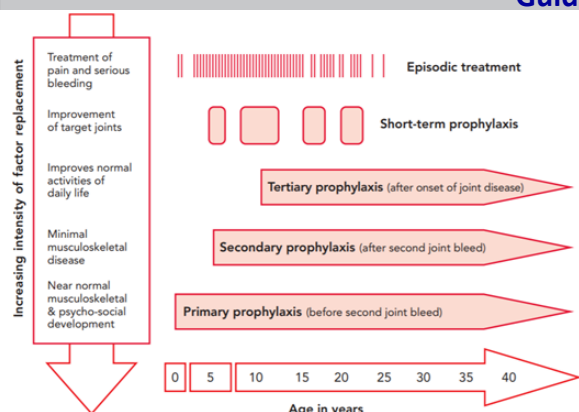
When bleeding is not controlled, it can lead to life-threatening emergencies. Serious problems occur when the patient bleeds into joints, muscles, and mucous membranes. This can cause extreme pain and permanent damage, eventually causing the patient to need surgery. Life-threatening bleeds include intracranial, neck/throat, and gastrointestinal.

Laboratory tests can help in the diagnosis of the condition. The following results are typical in the presence of Hemophilia A or B.

- **Prolonged activated partial thromboplastin time (aPTT):** both type A and B
 - Tests intrinsic and common pathways (factors XII, XI, IX, VIII, X, V, II, I)
- **Decreased factor VIII or IX:** provides a definitive diagnosis
- Normal prothrombin time (PT)
 - Tests extrinsic and common pathways (factors VII, X, V, II, I)
- Normal platelet
- Normal VWF
- Normal bleeding time

Hemophilia, cont.

Guideline Directed Treatment³



- **Episodic** ("on demand") treatment: active bleed
- **Intermittent ("periodic") short-term prophylaxis**: treatment to prevent bleeding for periods <45 weeks/year
- **Tertiary prophylaxis**: started after onset of joint disease
- **Secondary prophylaxis**: started after 2 or more bleeds into large joints (ankles, knees, hips, elbows, shoulders) and before joint disease documented
- **Continuous prophylaxis/primary prophylaxis**: started before a documented joint disease, before the second clinically evident large joint bleed, and before age 3

Guideline can be accessed at the following: <http://www1.wfh.org/publications/files/pdf-1472.pdf>

Treatment for Hemophilia Type A¹⁻⁷

Factor VIII Concentrates:

Replaces factor VIII

- Each U of FVIII concentrate/kg of body weight IV will raise plasma factor VIII levels by 2 IU/dL (2%)
- Dose calculation: Weight kg x desired rise in factor level %, multiply by 0.5
- Factor VIII replacement is necessary for clot formation and maintenance of hemostasis. It activates factor X in conjunction with activated factor IX. Activated factor X converts prothrombin to thrombin, which converts fibrinogen to fibrin, and with factor XIII forms a stable clot

Class	Agents	Half-life (hours)	Adverse Drug Reactions
Recombinant Factor VIII Concentrates	Advate, Adynovate, Afstyla, Eloctate, Kogenate FS, Kovaltry, Novoeight, Nuwiq, Recombinate, Xyntha, Xyntha Solofuse	11-20, depending on specific agent	Headache, pruritus, skin rash, urticaria, nausea, vomiting, arthralgia, cough, nasopharyngitis, fever
Human Plasma Derived Immunoaffinity-Purified Factor VIII Concentrates	Hemofil M	15	Allergic reactions, mild chills, nausea, or stinging at the infusion site
Human Plasma Derived Concentrates that Contain Factor VIII and VWF	Alphanate, Humate-P, Wilate, Koate-DVI	6-18, depending on the specific agent	Facial edema, nausea, hemorrhage, fever

Desmopressin (DDAVP, Stimate)

- Synthetic analogue of the antidiuretic hormone arginine vasopressin. In a dose dependent manner, desmopressin increases cyclic adenosine monophosphate (cAMP) in renal tubular cells which increases water permeability resulting in decreased urine volume and increased urine osmolality; increases plasma levels of von Willebrand factor, factor VIII, and t-PA contributing to a shortened activated partial thromboplastin time (aPTT) and bleeding time.
- Can be used in mild-moderate type A with factor activity >5% (not to be used in severe type A) and in carriers.
- Adverse Drug Reactions: xerostomia, hyponatremia
- Precautions:
 - Do not use in children younger than 2 years old
 - Do not use in severe renal impairment (CrCl <50 mL/min)
 - Caution during labor, eclampsia, and pre-eclampsia
 - Excessive water intake can cause hyponatremia and seizures
 - Tachyphylaxis can occur due to decrease in stored factor levels

Hemophilia, cont.

Bispecific antibody (Hemlibra)

- IgG 4 antibody with bispecific factor IXa and X directed antibody, bridges factor IX and X to restore function of factor VIII
- Common adverse drug reactions: headache, injection site reaction, arthralgia
- Cases of thrombotic microangiopathy and thrombotic events were reported when an average cumulative amount of > 100 units/kg/24 hours of activated prothrombin complex (aPCC) concentrate was administered for ≥ 24 hours to patients receiving emicizumab prophylaxis.

Agents for Acquired Hemophilia A (Obizur [VIII], NovoSeven RT [VIIa])

- Acquired hemophilia is seen with other autoimmune diseases
- Well-tolerated, no contraindications

Treatment for Hemophilia Type B¹⁻⁷

Factor IX Concentrates:

Replaces factor IX

- Plasma derived: each U per kg weight IV will raise level by 1 IU/dL
- Recombinant: each U per kg weight will raise level by 0.8 IU/dL (adults) 0.7 (children)
- Dose calculation: Weight kg x desired rise

Class	Agents	Half-life (hours)	Adverse Drug Reactions
Recombinant Factor IX Concentrates	Alprolix, BeneFix, Idelvion, Ixinity, Rebinyn, Rixubis	11-118, depending on specific agent	Dizziness, injection site reaction, antibody development, headache
Human Plasma Derived Factor IX Concentrates	AlphaNine SD, Mononine	21-25	Allergic reactions, thrombosis, chills, nausea, vomiting, diarrhea, increased liver function tests, fever, flushing, hypotension

Treatment for Hemophilia Type A or B¹⁻⁷

Bypassing agents (BPA)

Contain other factors that are able to bypass an inhibitor to factor VIII or IX

- APCCs are more effective than PCCs, and are preferred

Human Plasma Derived Activated Prothrombin Complex Concentrate (APCC) for Type A or B: FEIBA

Human Plasma Derived Prothrombin Complex Concentrate (PCC) for Type A or B: Profilnine SD: contains factors II > IX, X > VII, and X

Recombinant Factor VIIa Concentrate for Type A and B: NovoSeven RT: contains factor VIIa

Antifibrinolytics

Competitively blocks plasminogen to plasmin to prevent clot lysis

Tranexamic acid: (Cyklokapron, Lysteda) Good for menorrhagia and is given during menstruation, cannot administer with PCC due to thromboembolism risk, need to separate by at least 12 hours

Aminocaproic acid (EACA) (Amicar): used less often because it has a shorter half-life, is less potent, and more toxic; good for mucosal and mouth bleeds; clotting factor concentrate is given first, then EACA is given 6 hours later

For questions regarding coverage of hemophilia agents, please see the KDHE-DHCF Web Site at <http://www.kdheks.gov/hcf/>.

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Generic Medications

Recently Approved Generic Drugs:

May 2019	June 2019	July 2019
Sapropterin (Kuvan®) Sildenafil (Revatio®) solution	Dapsone (Aczone®) Tobramycin (Bethkis®)	Febuxostat (Uloric®) Icatibant (Firazyr®) Pregabalin (Lyrica®)

Upcoming Generic Drugs:

Generic Name	Brand Name	Anticipated Launch
Sodium Phosphate, Dibasic, Anhydrous; Sodium Phosphate,	Osmoprep®	November 16, 2019

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